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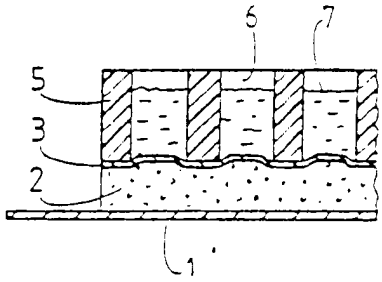
(54) TEST ASSEMBLY FOR BIOCHEMICAL ANALYSIS

(57) Test assembly for biochemical analysis by means of a membrane 3 onto which biological molecules are fixed by adsorption. Membrane 3 is attached onto a thin layer of synthetic foam 2, which is in turn attached onto a rigid support 1. A perforated plate 5 is applied with pressure onto membrane 3 so as to form wells 6 functioning as individual incubation chambers for diluted samples 7 to be analyzed. The test assembly permits conducting a large series of reactions in a rational manner.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The present invention has for a subject a test assembly for biochemical analysis by means of a membrane onto which biological molecules are fixed by adsorption.

The adsorption of proteins, nucleic acids and other biological molecules on solid supports is used in numerous techniques of biochemical analysis. Porous supports, presented in the form of membranes, permit adsorbing macromolecules by hydrophobic, electrostatic or covalent interactions. These membranes, however, are often fragile and difficult to handle.

In biochemical analyses where the reactions take place in solid phase, one generally looks for the presence, in the sample to be tested, of one or more molecules of a ligand capable of reacting with the biological macromolecules fixed on the membrane. The presence of the ligand is detected by means of a probe (radioactive, coupled to an enzyme, colored, fluorescent, etc.) either directly, or by competition. The majority of techniques require successive incubations alternating with washings. The same test is often conducted on a series of samples. In this case, it is important to note that, in general, only one of the incubations, that of the diluted material to be analyzed, is specific for a given sample. In contrast, during washings and other incubations, all the other tests are processed parallelly and in an identical manner.

For this purpose, plates of synthetic material of standardized dimensions are generally used, known under the name ELISA (Enzyme Linked Immunosorbent Assay) plates, in which 8 x 12 wells of 7 mm diameter are formed. The biological molecules are adsorbed by the plastic. All the steps of

the reaction take place individually in each well, which renders large-series analyses time-consuming and fastidious.

The object of the present invention is to offer a test assembly permitting testing a series of samples in a much more rational and rapid manner than with the known means.

The test assembly according to the invention is characterized by the fact that it comprises a rigid planar support onto which is attached a layer of synthetic foam with closed cells, of uniform thickness, on which the membrane itself is attached onto which the biological molecules are fixed by adsorption according to a particular geometric configuration, a perforated plate with cylindrical holes open on both ends and arranged according to a configuration corresponding to the configuration of biological molecules on the membrane, the perforated plate being designed to be applied and pressed onto the foam so as to form wells that do not communicate with one another.

The configuration according to which the biological molecules are fixed onto the membrane can be, for example, an assembly of parallel lines or a matrix of points to which the holes of the perforated plate correspond.

The test assembly according to the invention permits conducting a large series of reactions in a particularly rational manner. In comparison to the use of conventional ELISA on microplates, the test assembly according to the invention also presents several advantages:

The support can be cut to measure and adapted to the number of samples to be analyzed.

At the position of the wells which contain the sample, a signal is detected, which is specific for the ligand of the sample on the biological macromolecules fixed on the membrane, as well as background noise due to non-specific adsorptions of the ligand and other reagents in the zone of the membrane not containing the macromolecules specific to the test.

Reagents or macromolecules that permit controlling the functioning of the test can be applied onto the membrane.

After the specific incubation, all the samples are treated in parallel in common incubations, thus accelerating the manipulations by sparing pipetting steps and improving the comparison of results from different samples.

The results can be evaluated visually or by photometry.

The support can be kept for documentation.

The attached drawing shows, by way of example, one form of embodiment of the invention.

Figure 1 is a planar view of the rigid support with its membrane in which is schematically shown the distribution of biological macromolecules.

Figure 2 is an elevational and sectional view, in larger scale, of the support of Figure 1 and the perforated plate before its application onto the support.

Figure 3 is a planar view of the perforated plate applied onto the support.

Figure 4 is an elevational and sectional view, in larger scale, of the assembly shown in Figure 3.

Figure 5 shows the support after reaction.

The support shown in Figures 1 and 2 is made up of a rigid plate 1, preferably of synthetic material, which can be cut with a pair of scissors, and onto which is glued a layer of synthetic foam 2 with closed cells, of a thickness of 1.5 mm, adhesive on both of its surfaces, onto which is glued in turn a porous membrane 3. This porous membrane for example, is made up of a 0.2 μ nitrocellulose filter from SCHLEICHER and SCHUELL BA 83. The biological macromolecules fixed by adsorption onto porous membrane 3 are distributed according to parallel lines 4. Indications on the nature and the position of biological macromolecules are inscribed on the free part of plate 1.

The test assembly also comprises a plate 5 of synthetic material pierced with parallel cylindrical holes 6 arranged in a matrix, the distance separating the rows of holes corresponding to the distance between two lines 4 of the macromolecules on the support. The density of the foam as well as the density of the subassembly comprised of plate 1, foam 2 and membrane 3 is less than 1 g/cm^3 so as to permit the assembly of elements 1, 2 and 3 to float on the surface of the liquid during non-specific incubations, thus minimizing the quantity of reagents necessary for the incubations.

In order to conduct the specific incubation of the samples, perforated plate 5 is applied onto porous membrane 3, by holding it pressed onto the support, as shown in Figure 4, so as to form wells 6 completely separate from one another; foam 2, which is compressed, assures the tight seal at the end of the holes of the plate, to prevent contamination of one sample by another during the specific incubation. The pressure can be supplied by an ordinary pair of spring clamps.

The samples to be analyzed are introduced in diluted form 7 into each of wells 6, which function as individual incubation chambers for the different samples to be analyzed.

After the specific incubation, the matrix of tubes 5 is separated from support 1 and the latter is then incubated with reagents common to all the samples (washings, conjugates, substrates, etc.) For this purpose, the support and its membrane are inverted, membrane 3 toward the bottom, on the top of appropriate reagents on which support 1 and membrane 3 float due to the low density of foam 2.

The result is read visually or by photometry by evaluating the reaction having occurred in the zone where the biological macromolecules are adsorbed. This visualization is illustrated in Figure 5, where colored segments 8, 9, 10 and 11 corresponding to specific wells 6 are shown. If the reaction has also occurred on control molecules applied to other configurations on the membrane, the good functioning of the test can be judged.

The assembly according to the invention is susceptible to numerous variations of embodiment. In particular, the biological macromolecules could be fixed onto membrane 3 according to a matrix of points corresponding to the matrix of holes of perforated plate 6 or according to any other particular configuration that would correspond to a similar configuration of holes. The perforated plate could also be made in another manner. Membrane 3 need not necessarily be porous; a non-porous film may be suitable.

CLAIMS

1. Test assembly for biochemical analysis by means of a membrane onto which biological molecules are fixed by adsorption, characterized by the fact that it comprises, on the one hand, a rigid planar support (1) onto which is attached a layer of synthetic foam (2) with closed cells, of uniform thickness, onto which said membrane (3) is attached in turn, onto which the biological molecules are fixed by adsorption according to a particular geometric configuration (4), and, on the other hand, a plate perforated with cylindrical holes (5, 6) open on both of their ends and arranged according to a configuration corresponding to the configuration of the biological molecules on the perforated plate, and this perforated plate is designed to be applied and pressed onto the foam so as to form wells (6) that do not communicate with one another.

2. Assembly according to claim 1, further characterized by the fact that the configuration of biological molecules adsorbed is a collection of straight parallel lines (4) and that the configuration of holes (6) is a matrix whose rows correspond to said straight lines.

3. Assembly according to claim 1, further characterized by the fact that the configuration of biological molecules adsorbed is a matrix of points and that the configuration of holes is a similar matrix.

4. Assembly according to claims 2 or 3, further characterized by the fact that the rigid rectangular support (1) laterally projects beyond the foam, the

projecting edge (1a) bearing indications on the nature and the position of biological macromolecules fixed onto the membrane.

5. Assembly according to one of claims 1 to 4, further characterized by the fact that the density of the subassembly constituted by the rigid plate, the foam and the membrane is less than the density of water.

Single Sheet

In figs: Antigène = antigen

Fig.1

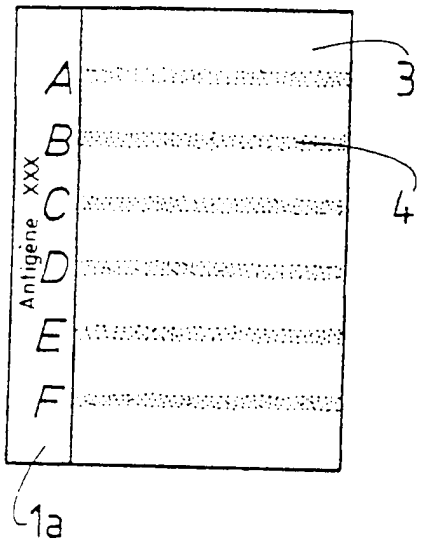


Fig.2

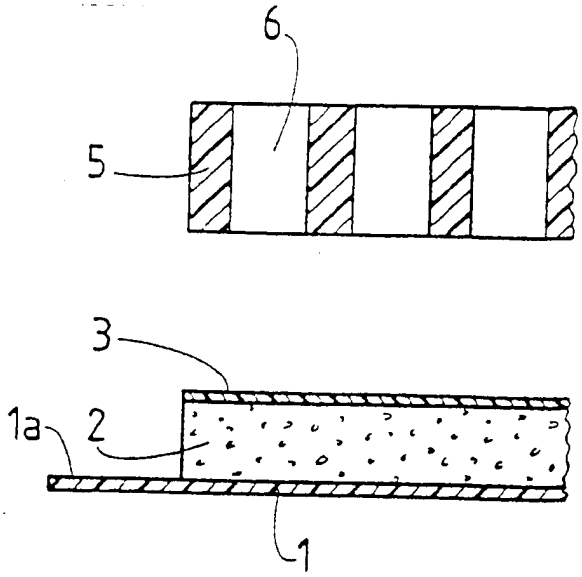


Fig.3

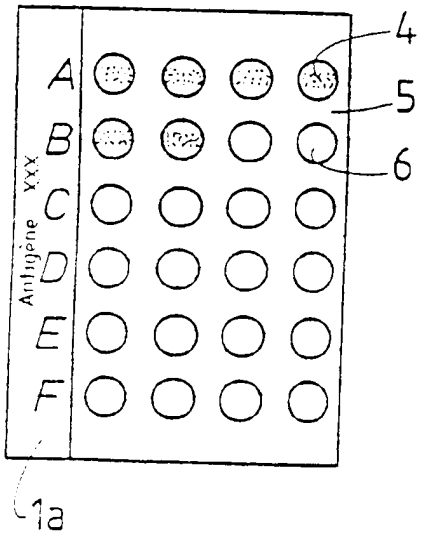
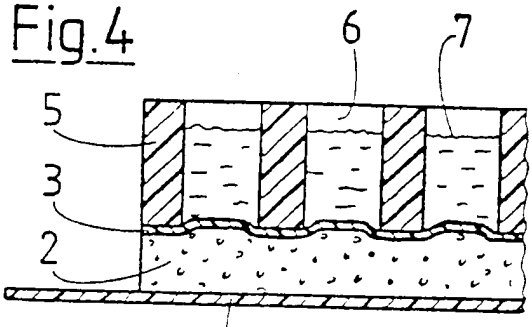


Fig.4



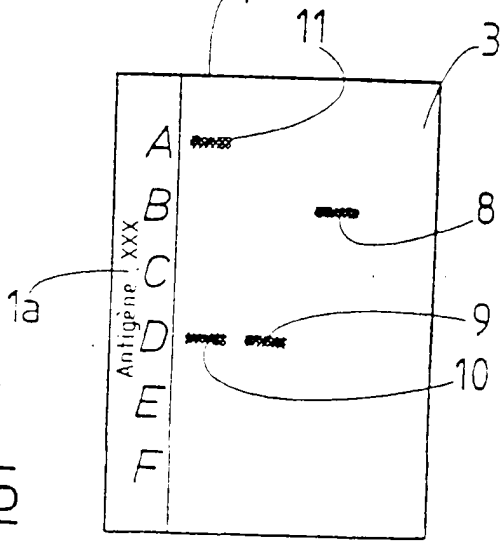


Fig.5